Pediatr Infect Vaccine. 2024 Apr;31(1):83-93
https://doi.org/10.14776/piv.2024.31.e13
pISSN 2384-1079·eISSN 2384-1087

PIV PEDIATRIC INFECTION & VACCINE

Original Article

Check for updates

Comparison of the Clinical and Laboratory Features of COVID-19 in Children During All Waves of the Epidemic: A Single Center Retrospective Study

Sunbok Suh, Hyungsu Kim

Department of Pediatrics, Busan Medical Center, Busan, the Republic of Korea

OPEN ACCESS

Received: Nov 8, 2023
Revised: Dec 3, 2023
Accepted: Dec 20, 2023
Published online: Feb 27, 2024

Correspondence to
Hyungsu Kim
Department of Pediatrics, Busan Medical Center, 359 World cup-daero, Yeonje-gu, Busan 47527, the Republic of Korea.
Email: h660216@hanmail.net

© 2024 The Korean Society of Pediatric Infectious Diseases
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs
Sunbok Suh
https://orcid.org/0009-0002-9397-2206
Hyungsu Kim
https://orcid.org/0009-0004-8923-6454

Funding
This work was supported by Public Medical Research Institute, Busan Medical Center.

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: Kim H; Data curation: Kim H, Suh S; Formal analysis: Kim H; Funding

ABSTRACT

Purpose: Since the start of the coronavirus disease 2019 (COVID-19) pandemic, various variants of concern have emerged. We divided the representative COVID-19 mutation period into four waves and aimed to analyze the clinical and laboratory features of children with COVID-19 from pre-mutation wave to the middle of omicron wave.
Methods: We retrospectively reviewed the medical records of hospitalized patients aged ≤19 years with laboratory confirmed COVID-19. Clinical and laboratory findings during pre-mutation (February 1st 2020 to September 30th 2020), alpha/beta (October 1st 2020 to May 31st 2021), delta (June 1st 2021 to October 31st 2021), and omicron (November 1st 2021 to May 31st 2022) waves were compared.
Results: Among total 827 patients, 163 (19.7%) were asymptomatic, and the frequency of fever and cough was 320 (38.7%) and 399 (48.2%), respectively. The proportion of fever ≥38.5°C was observed to be high during the omicron wave in the age group under 12 years. Lymphopenia was observed highly in the omicron wave in the age group under 12 years, and in the delta wave in the age group older than 12 years. Neutropenia was highly observed in the delta wave in the 0–4 years age group.
Conclusions: There were distinct characteristics during all epidemic waves of COVID-19. Children with COVID-19 had more frequent persistent fever during delta wave and children during the omicron wave had a higher peak fever.

Keywords: COVID-19; SARS-CoV-2; Children; Neutropenia; Lymphopenia

INTRODUCTION

Since the declaration of coronavirus disease 2019 (COVID-19) as a pandemic in March 2020 by the World Health Organization, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has continued to spread rapidly, resulting in >34 million cases South Korea by September 17, 2023.[1] In the past 3 years, numerous viral variants have been characterized, variants of concerns (VOCs) have been associated with increased transmissibility, evasion of immunity from infection and vaccination, and reduced efficacy of public health measures.[2,3] Representative VOCs of SARS-CoV-2 were alpha variant (B.1.1.7), beta variant (B.1.351), delta variant (B.1.617.2) and omicron varinat (B.1.1.529).[4,5] According to reports so far, delta VOC

Generated by Xmlinkpress

acquisition: Kim H; Investigation: Kim H; Methodology: Kim H; Project administration: Kim H; Resources: Kim H; Software: Kim H; Supervision: Kim H; Validation: Kim H, Suh S; Visualization: Kim H; Writing - original draft: Kim H; Writing - review & editing: Kim H, Suh S.

was associated with increased severity of illness, longer viral shedding and high intensive care unit admission rate. But, emergence of omicron VOC was characterized as less involvement of the lower respiratory tract and reduced probability of hospital admission. And a rapid increase in croup and febrile convulsion cases was observed during omicron wave.[6,7]

Data on the laboratory features of each wave in children are limited. But, so far the most common WBC abnormalities in children with COVID-19 were leukopenia and lymphopenia.[8] Data on children with COVID-19 have shown no abnormalities in red blood cell count, level of hemoglobin.[9]

This study aimed to examine the clinical and laboratory characteristics of hospitalized patients with COVID-19 in children and adolescents under the age of 19 experienced at a single center from the beginning of pre-mutation wave to omicron wave in May 2022.

MATERIALS AND METHODS

1. Subjects and definitions

In this study, pediatric patients aged 19 or younger hospitalized at Busan Medical Center due to SARS-CoV-2 infection from February 1st 2020 to May 31st 2022 were included. During the study period, mandatory quarantine was being implemented at medical institutions or residential treatment centers for newly confirmed COVID-19 patients in the region where the research institute belongs. The research institution was a medical center dedicated to COVID-19 pandemic, and decisions on assignment for hospitalizations during the study period were made by the local health authorities. There was no difference according to age group in the selection of patients' hospitalization institutions. Throughout the entire epidemic period, severe patients in the region were assigned to tertiary general hospitals, and moderate and mild patients were assigned to our institution. After the middle of the omicron period, inpatients were allocated evenly among general hospitals in the region. SARS-CoV-2 infection was defined as a positive result from a polymerase chain reaction test on a nasopharyngeal sample. The research period was divided into 4 VOC waves according to the pre-mutation period of the new COVID-19 virus and the VOC dominance period. Each wave was determined by combining the time of first discovery of VOC viruses and the time of maximum detection of VOC viruses in Korea.[2,10,11]

Patients were divided into four waves as follows, depending on the time the patient was diagnosed with COVID-19: Pre-mutation wave from February 1st 2020 to September 30th 2020, alpha/beta variants of concern wave from October 1st 2020 to May 31st 2021, delta variant of concern wave from June 1st 2021 to October 31st 2021, and omicron variant of concern wave from November 1st 2021 to May 31st 2022.

Identification of transmission routes was based on epidemiological investigation data from public health centers or, in some cases that were missing, based on medical history data from patients and guardians.

The severity of COVID-19 infection was classified as mild, moderate and severe. Mild COVID-19 patients were defined as patients who did not require oxygen supply, while moderate COVID-19 patients were defined as patients who required oxygen supply and severe COVID-19 patients as patients requiring non-invasive or invasive mechanical ventilation.

https://doi.org/10.14776/piv.2024.31.e13

Fever was defined as 38°C or higher.[4] Patients were classified into 3 age groups: 0–4 years group, 5–11 years group, and 12–19 years group. In clinical diagnosis, pneumonia was defined as the presence of symptoms or signs indicative of pneumonia, including cough, abnormal auscultation findings and lung infiltration on chest radiographs. The bronchiolitis was diagnosed when a child had tachypnea, intercostal retraction, prolongation of expiration, wheezing and hyperinflation on chest radiographs. The croup was diagnosed when a child had a barky cough and stridor, and febrile seizure was defined when a child had a convulsion while in a febrile state.

Laboratory findings were analyzed using whole blood samples taken within the hospitalization period, and meaningful measurements were analyzed when performed more than twice. In laboratory findings, leukopenia was defined as a total white blood cell count <4,000/μL and lymphopenia or neutropenia was defined as the counts <1,500/μL. Thrombocytopenia was defined as the counts <150,000/μL and cutoff of liver transaminase level was defined as more than 3 times the upper limit of normal level. C-reactive protein (CRP) was considered elevated when level ≥0.5 mg/dL. Lactate dehydrogenase (LDH) elevation was set to over 500 IU/L in children under 10 years of age and over 330 IU/L in children over 10 years of age.

2. Data collection and statistical analysis

The medical records of the study subjects were analyzed retrospectively. For SARS-CoV-2 infection, the exposure route, presence of symptoms, severity, duration of fever, peak fever and laboratory findings were investigated. Epidemiological, clinical and laboratory features were compared according to waves of VOC during the study period.

To compare between subjects according to waves of COVID-19 infection, Fisher's exact test and χ^2 tests were performed on non-continuous variables, while the Mann-Whitney *U* test was performed for non-normally distributed continuous variables and independent group *t*-test for normally distributed continuous variables. *P*-value less than 0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

3. Research ethics

This study was approved by the Institutional Review Board of Busan Medical Center (IRB No. 2022-06-002).

RESULTS

1. Demographics characteristics

A total of 827 patients were included in the analysis: 32 in pre-mutation wave, 168 in alpha/beta wave, 318 in delta wave, and 309 in omicron wave. The median age of all patients was 10 years (range, 1–18 years), 465 (56.2%) were male and 362 (43.8%) were female. The oldest average age of the target children was median 15 years (range, 4–19 years) old in pre-mutation wave, and the youngest was median 8 years (range, 1–18 years) old in omicron wave. In terms of age distribution, the 12–19 years group had the largest number of patients with 349 (42.2%), followed by the 5–11 years group with 325 (39.3%). In omicron wave, the proportion of patients in the 0–4 years group and the 5–11 years group was high (27.5% and 42.1%, respectively). In contrast, the proportion of 12- to 19- years old patients were high in alpha/beta and delta waves. (49.4% and 47.5%, respectively) (**Table 1**, **Fig. 1**).

https://doi.org/10.14776/piv.2024.31.e13

PIV PEDIATRIC INFECTION & VACCINE

Table 1. Demographics of 827 children with COVID-19 during the study period

Characteristics	Total (n=827)	Pre-mutation wave (n=32)	Alpha and beta wave (n=168)	Delta wave (n=318)	Omicron wave (n=309)	*P*-value		
						Overall	Alpha/beta vs. Delta	Delta vs. Omicron
Age (yr)	10 (1–18)	15 (4–21)	11 (2–18)	10 (1–18)	8 (1–18)	0.00*	0.479†	0.00†
Sex						0.19‡	0.12‡	0.46‡
Female	362 (43.8)	12 (37.5)	85 (50.6)	139 (43.7)	126 (40.8)			
Male	465 (56.2)	20 (62.5)	83 (49.4)	179 (56.3)	183 (59.2)			
Age group (yr)						0.00‡	0.49‡	0.00‡
0–4	153 (18.5)	2 (6.3)	26 (15.5)	40 (12.6)	85 (27.5)			
5–11	325 (39.3)	9 (28.1)	59 (35.1)	127 (39.9)	130 (42.1)			
12–19	349 (42.2)	21 (65.6)	83 (49.4)	151 (47.5)	94 (30.4)			

Data shown are median (range) or number of hospitalized COVID-19 cases (%).
Abbreviation: COVID-19, coronavirus disease 2019.
Continuous variables were analyzed using *Mann-Whitney *U* test or †Independent *t* -test. Categorical variables were analyzed using ‡χ^2 test.

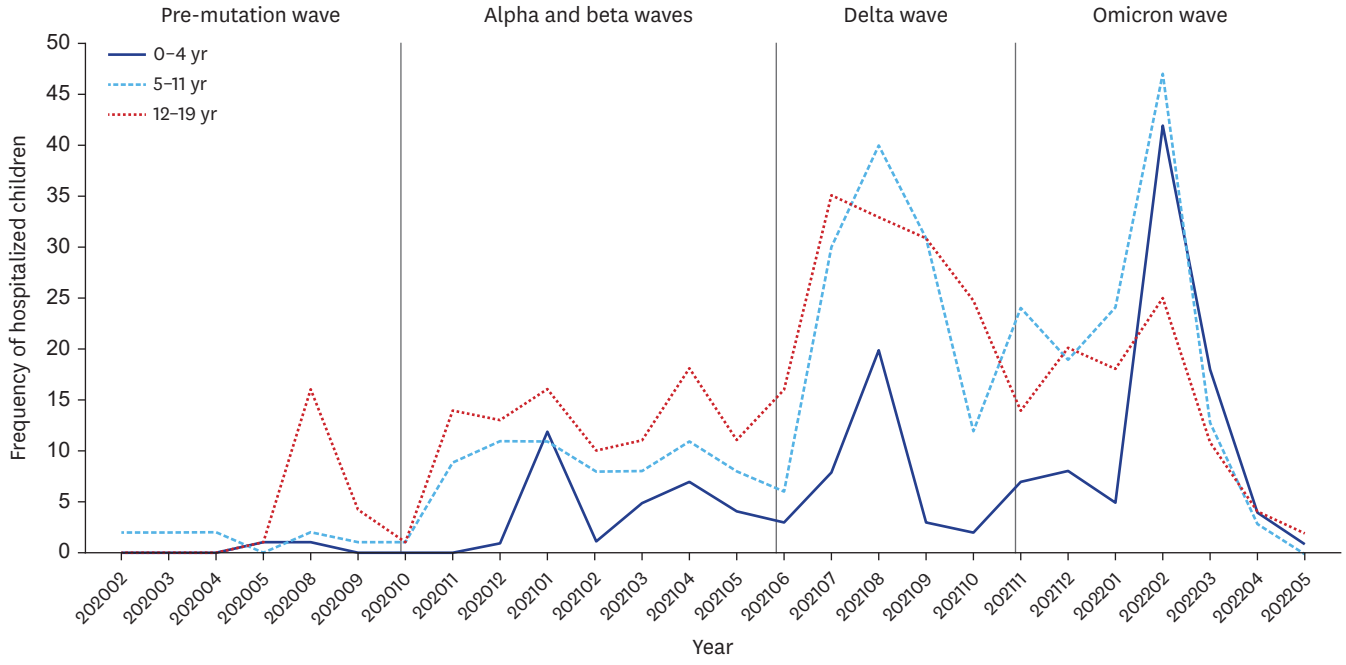

Fig. 1. Number of coronavirus disease 2019 hospitalized children according to age group over time.

2. Epidemiologic characteristics

During the entire waves, household transmission was 56%, and differences were observed depending on each wave (P<0.001). Transmission in educational facilities was the second highest at 19.6% and the transmission route was unknown in 14.1% of cases. And transmission due to contact with relatives or acquaintances was 7.2%. When analyzing the exposure route according to age group, household transmission was observed at 24.6%, 42.5% and 32.8% in the 0–4 years group, 5–11 years group and 12–19 years group, respectively. Cases of extrafamilial transmission were confirmed to be 11.9%, 27.1% and 61% in the 0–4 years group, 5–12 years group and 12–19 years group, respectively (**Fig. 2**).

3. Clinical features

Of the total 827 patients, 163 (19.7%) were asymptomatic during hospitalization, and the proportion of asymptomatic patients was high in alpha/beta waves and delta wave (44.8% and 34.4%, respectively). The most common symptoms of symptomatic children were cough (48.2%), fever (38.7%), sore throat (21.5%), runny nose (13.4%) and headache (10.3%). The

https://doi.org/10.14776/piv.2024.31.e13

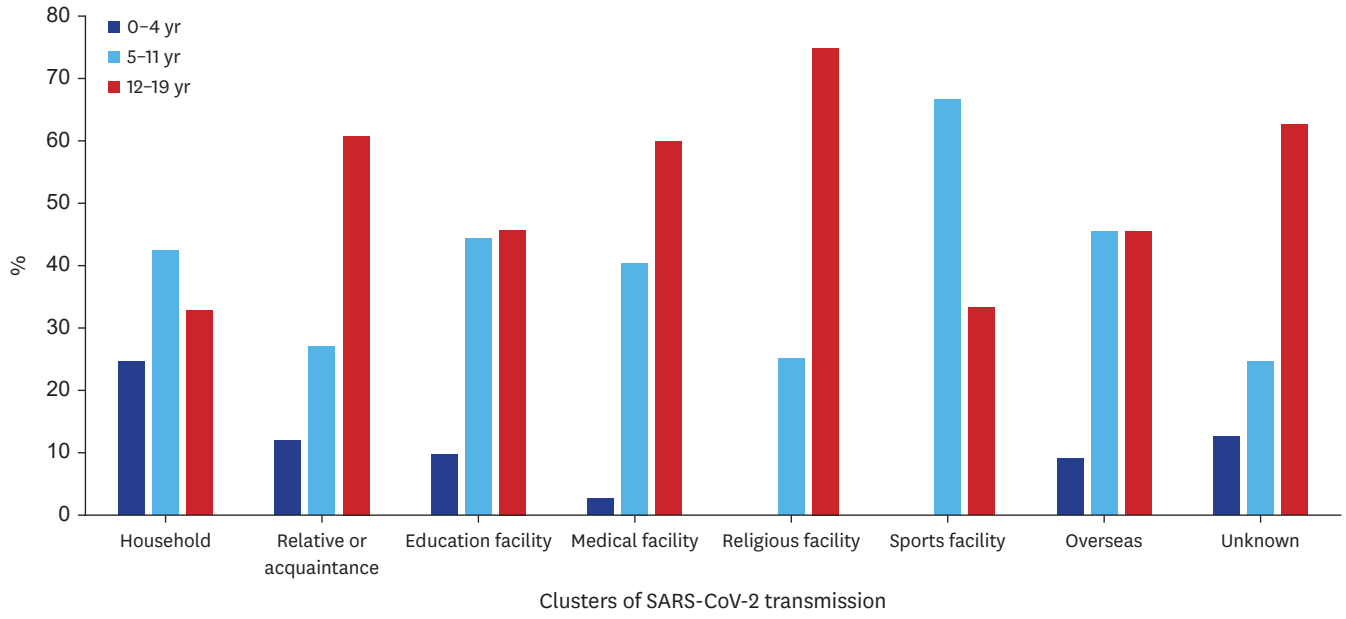

Fig. 2. Clusters of SARS-CoV-2 transmission according to age distribution.
Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

frequency of fever was high in delta wave and omicron wave (36.6% and 50.9%, respectively). The frequency of coughing was also high in delta wave and omicron wave (38.1% and 49.6%, respectively). There was no difference in severity among waves of variants of concern (P=0.664).

The peak fever recorded above 38.5°C was higher in omicron wave (27.8%) than in alpha/beta waves (3.57%) or delta wave (17.3%) (P<0.001). The proportion of patients who had fever for more than 4 days was the highest at 5% in delta wave, followed by 3.1% and 3.56% in pre-mutation and omicron waves, respectively (P=0.03). The average duration of fever was 2 to 3 days during all waves, with no significant differences (P=0.3) (**Table 2**).

By the characteristics of fever according to age group, fever was more common in the 5 years or older group than the 0–4 years group (39.7% vs. 23.4%, P=0.006), and cough was more common in the 12–19 years group than the 0–4 years group. (44.9% vs. 18.8%, P=0.218). The proportion of pneumonia increased to 18.9% in the delta wave, and croup increased to 5.2% in the omicron wave (P<0.001).

4. Laboratory abnormalities

Leukopenia, lymphopenia, neutropenia, and thrombocytopenia were observed in 276 patients (33.4%), 304 patients (36.8%), 206 patients (24.9%) and 43 patients (5.2%), respectively. Liver transaminases were elevated in 3.2% of all patients, and CRP and LDH was elevated in 16% and 2.6%. Leukopenia, neutropenia, lymphopenia and elevation of liver transaminases did not show differences depending on each wave (**Table 3**). When compared by age group, leukopenia in the 5–11 years group was 43.4% in omicron wave, which was statistically significantly higher than that in alpha/beta wave and delta wave (P<0.001). Additionally, lymphopenia in the 5–11 years group was also statistically significantly higher at 44.2% in omicron wave (P<0.001). In the 12–19 years group, thrombocytopenia was observed at a high rate of 11.9% in delta wave (P<0.05) (**Fig. 3**).

https://doi.org/10.14776/piv.2024.31.e13

Table 2. Clinical manifestations of hospitalized children with COVID-19 during study period

Variables	Total (n=827)	Pre-mutation wave (n=32)	Alpha and beta wave (n=168)	Delta wave (n=318)	Omicron wave (n=309)	*P*-value		
						Overall	Alpha/beta vs. Delta	Delta vs. Omicron
Fever peak (°C)	38.6 (38.0–40.2)	38.6 (38.3–38.9)	38.4 (38.0–40.2)	38.5 (38.0–40.2)	38.7 (38.0–40.2)	0.003*	0.00†	0.02†
Fever peak ≥38.5°C	148 (17.8)	1 (3.1)	6 (3.6)	55 (17.3)	86 (27.9)	0.00§	0.00§	0.001§
Fever duration (day)	2 (1–8)	3 (1–7)	2 (1–8)	2 (1–7)	2 (1–8)	0.3§	0.00§	0.738§
Fever ≥4 days	29 (3.5)	1 (3.1)	1 (0.2)	16 (5)	11 (3.6)	0.03§	0.003§	0.364§
Clinical symptom								
Asymptomatic	163 (19.7)	10 (31.3)	73 (43.5)	56 (17.6)	24 (7.8)	<0.001‡	0.00‡	0.00‡
Fever	320 (38.7)	9 (28.1)	31 (18.5)	117 (36.8)	163 (52.8)	<0.001‡	0.008‡	0.00‡
Coughing	399 (48.2)	3 (9.4)	46 (27.4)	152 (47.8)	198 (64.1)	<0.001‡	0.00‡	0.00‡
Rhinorrhea	111 (13.4)	0 (0)	15 (8.9)	32 (10.1)	64 (20.7)	<0.001‡	0.687‡	0.00‡
Headache	85 (10.3)	7 (21.9)	12 (7.1)	35 (11.0)	31 (10.0)	0.08‡	0.171‡	0.691‡
Sore throat	178 (21.5)	6 (18.8)	23 (13.7)	77 (24.2)	72 (23.3)	0.04‡	0.006‡	0.788‡
Clinical diagnosis								
Pneumonia	102 (12.3)	7 (21.9)	6 (3.6)	60 (18.9)	29 (9.4)	0.0‡	0.0‡	0.001‡
Bronchiolitis	15 (1.8)	0 (0)	4 (2.4)	6 (1.9)	5 (1.6)	0.7§	0.743§	0.752§
Croup	19 (2.3)	0 (0)	0 (0)	3 (0.9)	16 (5.2)	0.0§	0.32§	0.002§
Febrile convulsion	5 (0.6)	0 (0)	0 (0)	2 (0.6)	3 (1.0)	0.443§	1.0§	0.367§
COVID-19 severity						0.66‡	0.354‡	0.963‡
Mild	815 (98)	31 (96)	167 (99.4)	313 (98.4)	304 (98.3)			
Moderate	12 (1.4)	1 (3.1)	1 (0.5)	5 (1.5)	5 (1.6)			
Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)			

Data shown are median (range) or number of hospitalized COVID-19 cases (%).
Abbreviation: COVID-19, coronavirus disease 2019.
Continuous variables were analyzing using *Mann-Whitney *U* test or †Independent *t*-test. Categorical variables were analyzed using ‡χ^2 test or §Fisher's exact test.

Table 3. Laboratory findings of children with COVID-19 from February 1st 2020 to May 31st 2022

Laboratory findings	Total (n=827)	Pre-mutation wave (n=32)	Alpha and beta wave (n=168)	Delta wave (n=318)	Omicron wave (n=309)	*P*-value		
						Overall	Alpha/beta vs. Delta	Delta vs. Omicron
Leukopenia	276 (33.4)	8 (25.0)	43 (25.6)	114 (35.9)	111 (35.9)	0.06*	0.022*	0.985*
Lymphopenia	304 (36.8)	12 (37.5)	49 (29.2)	115 (36.2)	128 (41.4)	0.07*	0.121*	0.176*
Neutropenia	206 (24.9)	4 (12.5)	33 (19.6)	85 (26.7)	84 (27.2)	0.88*	0.083*	0.898*
Thrombocytopenia	43 (5.1)	0 (0.0)	2 (1.2)	21 (6.6)	20 (6.5)	0.02†	0.008*	0.947*
Elevated liver transaminases	27 (3.2)	3 (9.4)	8 (4.8)	6 (1.9)	10 (3.2)	0.07†	0.072†	0.284*
CRP elevation	136 (16.4)	5 (15.6)	13 (7.7)	35 (11.0)	83 (26.9)	<0.001*	0.251*	0.000*
LDH elevation	22 (2.7)	4 (12.5)	4 (2.4)	6 (1.9)	8 (2.6)	0.005†	0.743†	0.59†

Data shown are number of hospitalized COVID-19 cases (%).
Abbreviations: COVID-19, coronavirus disease 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase.
Categorical variables were analyzed using *χ^2 test or †Fisher's exact test.

DISCUSSION

A total of 827 COVID-19 pediatric patients hospitalized at a single center were included in the analysis. For the age group, our study found that the proportion of the 12–19 years group was higher than those of other years groups. The average age of each wave was the highest at 15 years in the pre-mutation wave and the lowest at 8 years in omicron wave. There were more male patients than female patients in all age groups, but this was not statistically significant.

In this study, we found that the number of affected subjects was the highest during the omicron wave in the 0–4 years group, while the number were evenly high in the delta wave and the omicron wave in the 5–11 years group and in the delta wave in the 12–19 years group, which was consistent with previous findings.[12] For the epidemiological characteristics, intra-household transmission accounted for 56% of the total transmission route, which was

https://doi.org/10.14776/piv.2024.31.e13

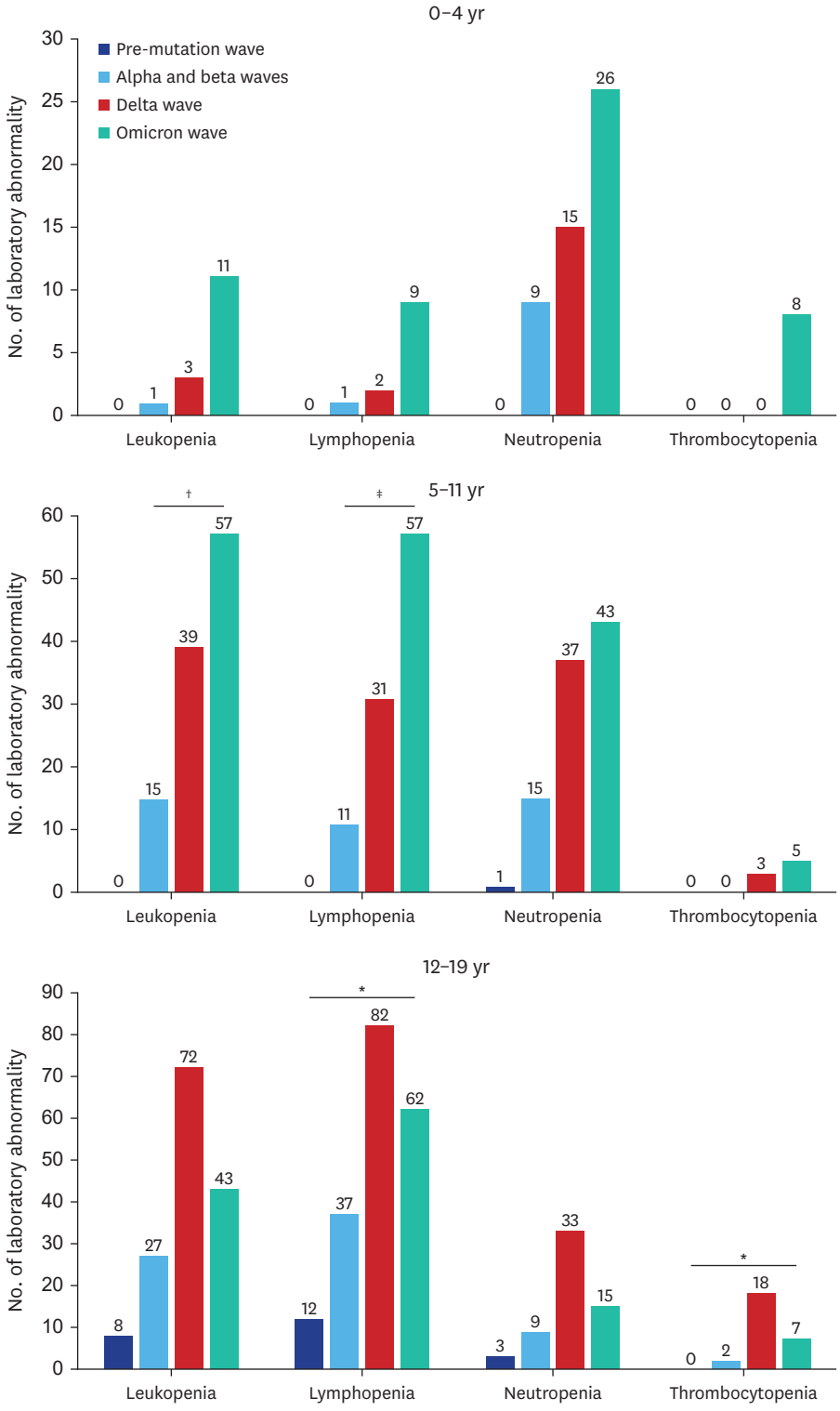

Fig. 3. Number of laboratory abnormality during all waves in children 0–4 years, 5–11 years, and 12–19 years with coronavirus disease 2019.
*P<0.05, †P<0.01, and ‡P<0.001.

https://doi.org/10.14776/piv.2024.31.e13

consistent with a previous report from a domestic multicenter study that showed 61.6% of intra-household transmission among hospitalized children under 12 years of age.[13] And also, reports in Israel and Singapore found that the secondary incidence rate of COVID-19 was lower in infants than in other age groups.[14,15] By age groups, we also revealed that the rate of intra-household transmission was higher in the age group of 5 years and older than in the age group of 0–4 years, which was consistent with previous studies on intra-household transmission of COVID-19 in children.

For the clinical characteristics, the proportion of asymptomatic patients during hospitalization was found to be 19.7%, which was a low rate compared to the 34.1% and 34.4% reported by the domestic multicenter study and the Korea Disease Control and Prevention Agency (KDCA) for those aged under 18.[13,16] The reason for the difference in the proportion of asymptomatic patients in various reports was assumed to be the difference in whether patients with very mild symptoms were considered as asymptomatic or symptomatic. The frequency of the main symptoms was 48.2% and 38.7% for cough and fever, respectively, which was inconsistent from the previous multicenter study report in which the main symptoms included fever and cough in the order, but the frequency of rhinorrhea, headache and sore throat were found to be similar.[13] For fever, one of the main systemic symptoms, a high frequency of the maximum body temperature being 38.5°C or higher was found during the omicron wave, and a high frequency of fever persisting for more than 4 days was observed during the delta wave. Marks et al.[17] reported that in the delta wave, oxygen treatment and intensive care were more frequently required and inflammatory markers were higher, while in the omicron wave, the hospitalization rate was found to be lower with relatively shorter hospitalization period, but febrile convulsions being more frequent due to higher occurrence of fever of 38.5°C or higher. In a report by the KDCA on the VOC waves, it is shown that in the age group 19 years or younger, the severity rate and fatality rate were reported to be 0.04% in delta wave, which was higher than that of omicron wave, 0.01% or less.[3] The fact that there were many cases of fever lasting more than 4 days during delta wave seems to be related to increase in fatality rate as the fever lasts for a long time.

The proportion of patients with fever and cough in the 5-years or older group was shown to be higher than that in the 0–4 years group, which was partly inconsistent with the previous report that the rate of main symptoms by age group was higher in the younger age group.[15] It was presumed that this was probably due to the dispersion of younger age patients due to changes in hospitalization policy during omicron wave. The proportion of patients with fever persisting more than 4 days and a maximum body temperature of more than 38.5°C were similar between all age groups, but in the 0–4 years group and the 5–11 years group, the proportion of patients with the highest body temperature being higher than 38.5°C was found to be high during the omicron wave. On the other hand, in the 12–19 years group, the proportion of patients with fever persisting more than 4 days was found to be high in the delta wave. These findings were correlated with the clinical diagnosis of this study, where croup and febrile seizure were high in the omicron wave and pneumonia was high in the delta wave (**Table 4**). Also, these could be understood in the same context in that moderate cases were more common in delta and omicron waves, which were commonly observed in the 12–19 years group.[18,19]

Among the laboratory findings, no significant differences were found between all waves in occurrence of leukopenia, lymphopenia, neutropenia and abnormality in liver function test, while there were significant differences in occurrence of thrombocytopenia, CRP and LDH

https://doi.org/10.14776/piv.2024.31.e13

Table 4. Clinical features according to degree and duration of fever between age groups

Age groups	Pre-mutation wave	Alpha/beta wave	Delta wave	Omicron wave	*P*-value
0–4 years group					
Fever peak ≥38.5°C	0 (0.0)	1 (3.8)	13 (32.5)	32 (37.6)	0.008*
Fever ≥4 days	0 (0.0)	0 (0.0)	2 (5.0)	6 (7.1)	0.547*
5–11 years group					
Fever peak ≥38.5°C	0 (0.0)	1 (1.7)	16 (12.6)	33 (25.4)	0.00*
Fever ≥4 days	0 (0.0)	0 (0.0)	3 (2.4)	2 (1.5)	0.657*
12–19 years group					
Fever peak ≥38.5°C	1 (5)	2 (2.4)	23 (15.2)	20 (21.3)	0.001*
Fever ≥4 days	1 (5)	0 (0.0)	11 (7.3)	3 (3.2)	0.063*

Categorical variables were analyzed using *Fisher's exact test.

elevation. Zheng et al.[20] reported that for laboratory findings for COVID-19, lymphopenia and leukopenia are the most common findings in pediatric patients and Liao et al.[21] reported that the degree of lymphopenia and thrombocytopenia is related to the severity of the disease. In this study, leukopenia and neutropenia were observed in 33% and 24.9% of occurrence, respectively, similar to previous reports.[4] The frequency of lymphopenia was observed at 30.2%, which was similar to the former pediatric studies. Yang et al.[22] reported that lymphopenia was observed in 80% of severe cases in adult patients with COVID-19. The occurrence of lymphopenia is explained with mechanism in which with the angiotensin converting enzyme 2 (ACE2) receptor being expressed on the surface of lymphocytes, SARS-CoV-2 infects through the receptor.[23] However, ACE2 is less developed in lymphocytes in pediatric population, and thereby the frequency of lymphopenia is much lower than in adults, which explains the favorable prognosis of children from COVID-19.[24] In this study, the differences in the proportion of children with leukopenia and lymphopenia according to age group were observed, which was found to be high at the omicron wave in both the 0–4 years group and the 5–11 years group, and the frequency of leukopenia and lymphopenia were observed to be high during the delta and omicron waves in the 12–19 years group. The high frequency of lymphopenia in the 0–4 years group and the 5–11 years age group is presumed to be a result of immunological immaturity and differences in reactivity to infection and virus sensitivity, but further research is needed.[25] Neutropenia was observed at the highest frequency in the 0–4 years group during the delta wave, which was consistent with previous studies showing that transient neutropenia is common in various viral infections in young age groups and is associated with severity.[26-28] It could be conclusively assumed that clinical severity and age may affect leukocyte abnormalities.

This study still contains several limitations. First, it was a retrospective study at a single center in a specific region, and there was a limitation in explaining the general characteristics of COVID-19 infection. Second, there was a possibility that other VOC may have been included in the wave of each variant of concern, and so the effects could not be accurately analyzed. Third, there were changes in standards for determination of hospitalization during the study period due to changes in quarantine policies and quarantine criteria for confirmed cases. Before the alpha and beta variants were dominant, patients were unconditionally quarantined and hospitalized when confirmed. But in the delta wave patients were initially quarantined at home or at a residential treatment center and were often hospitalized after the onset of symptoms, which limited the accurate analysis of clinical symptoms. Fourth, because our study was a single-center study and hospitalization was assigned by the local health authorities, the number of severe cases were small, which limited the evaluation of severity and overall analysis.

https://doi.org/10.14776/piv.2024.31.e13

In this study, significant differences in epidemiological characteristics, clinical symptoms and laboratory findings were found between epidemic waves and all age groups in pediatric patients with COVID-19 infection, which were similar or slightly different from previous reports of pediatric COVID-19 infection. Considering the high probability that SARS-CoV-2 infection in children will continue to further mutate and expand, it is necessary to further collect appropriate information on the disease pattern and clinical course. And thereby, further research is needed to manage SARS-CoV-2 infection in children and provide appropriate treatment guidelines.

REFERENCES

1. Korea Disease Control and Prevention Agency (KDCA). Surveillance status of COVID-19 positive cases [Internet]. Cheongju: KDCA; 2023 [cited 2023 Sep 17]. Available from: https://ncov.kdca.go.kr/bdBoardListR.do?brdId=1&brdGubun=11.
2. World Health Organization (WHO). Tracking SARS-CoV-2 variants [Internet]. Geneva: WHO; 2023 [cited 2023 Oct 8]. Available from: https://www.who.int/activities/tracking-SARS-CoV-2-variants.
3. Ryu BY, Shin EJ, Kim NY, Kim DH, Lee HJ, Kim AR. Severity of COVID-19 associated with SARS-CoV-2 variants circulating in the Republic of Korea. Public Health Wkly Rep. 2022;15:2873-83. CROSSREF
4. Han MS, Kim KM, Oh KJ, Chang JY, Lee SY, Choi JE, et al. Distinct clinical laboratory features of COVID-19 in children during the pre-delta, delta and omicron wave. Pediatr Infect Dis J 2023;42:423-8. PUBMED | CROSSREF
5. Ong SW, Chiew CJ, Ang LW, Mak TM, Cui L, Toh MP, et al. Clinical and virological features of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern: a retrospective cohort study comparing B.1.1.7 (alpha), B.1.351 (beta), and B.1.617.2 (delta). Clin Infect Dis 2022;75:e1128-36. PUBMED | CROSSREF
6. Maslo C, Friedland R, Toubkin M, Laubscher A, Akaloo T, Kama B. Characteristics and outcomes of hospitalized patients in South Africa during COVID-19 omicron wave compared with previous waves. JAMA 2022;327:583-4. PUBMED | CROSSREF
7. Menni C, Valdes AM, Polidori L, Antonelli M, Penamakuri S, Nogal A, et al. Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study. Lancet 2022;399:1618-24. PUBMED | CROSSREF
8. Ding Y, Yan H, Guo W. Clinical characteristics of children with COVID-19:a meta-analysis. Front Pediatr 2020;8:431. PUBMED | CROSSREF
9. Kosmeri C, Koumpis E, Tsabouri S, Siomou E, Makis A. Hematological manifestations of SARS-CoV-2 in children. Pediatr Blood Cancer 2020;67:e28745. PUBMED | CROSSREF
10. Kim IH, Park AK, Lee H, Kim J, Kim DH, Kim JA, et al. July 2021 status and characteristics of the COVID-19 variant virus outbreak in the republic of Korea. Public Health Wkly Rep 2021;14:3388-96.
11. Ahn S, Jang J, Park SY, Yang S, Ryu B, Shin E, et al. Outbreak report of COVID-19 during designation of class 1 infectious disease in the Republic of Korea (January 20, 2020–April 24, 2022). Public Health Wkly Rep 2022;15:2126-36.
12. Kang HM, Park JY, Choe YJ. Clinical manifestations, epidemiologic characteristics, and disease Burden of the coronavirus disease-19 in children ages 5-11 years old. Pediatr Infect Vaccine 2022;29:61-9. CROSSREF
13. Kim DH, Han MS, Kim HS, Lim MS, Choo MA, Lee E, et al. Establishment of multicenter cohort research system and analysis of clinical epidemiologic characteristics for children and adolescents with COVID-19. In: Proceedings of the 22th Congress of the Korean Society of Pediatric Infectious Diseases; 2021 Nov 20; Seoul, Korea. Seoul: Korean Society of Pediatric Infectious Diseases; 2021.
14. Somekh E, Gleyzer A, Heller E, Lopian M, Kashani-Ligumski L, Czeiger S, et al. The role of children in the dynamics of intra family coronavirus 2019 spread in densely populated area. Pediatr Infect Dis J 2020;39:e202-4. PUBMED | CROSSREF
15. Yung CF, Kam KQ, Chong CY, Nadua KD, Li J, Tan NW, et al. Household tranmission of severe acute respiratory syndrome coronavirus 2 from adult to children. J Pediatr 2020;225:249-51. PUBMED | CROSSREF
16. Choi SH, Kim HW, Kang JM, Kim DH, Cho EY. Epidemiology and clinical features of coronavirus disease 2019 in children. Clin Exp Pediatr 2020;63:125-32. PUBMED | CROSSREF

17. Marks KJ, Whitaker M, Anglin O, Milucky J, Patel K, Pham H, et al. Hospitalizations of children and adolescents with laboratory-confirmed COVID-19 –COVID-NET, 14 States. July 2021- January 2022. MMWR Morb Mortal Wkly Rep 2022;71:271-8. PUBMED | CROSSREF
18. Molteni E, Sudre CH, Canas LD, Bhopal SS, Hughes RC, Chen L, et al. Illness characteristics of COVID-19 in children infected with the SARS-CoV-2 delta variant. Children (Basel) 2022;9:652. PUBMED | CROSSREF
19. Shoji K, Akiyama T, Tsuzuki S, Matsunaga N, Asai Y, Suzuki S, et al. Comparison of the clinical characteristics and outcomes of COVID-19 in children before and after the emergence of delta variant of concern in Japan. J Infect Chemother 2022;28:591-4. PUBMED | CROSSREF
20. Zheng F, Liao C, Fan QH, Chen HB, Zhao XG, Xie ZG, et al. Clinical characteristics of children with coronavirus disease 2019 in Hubei, China. Curr Med Sci 2020;40:275-80. PUBMED | CROSSREF
21. Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. Lancet Haematol 2020;7:e671-8. PUBMED | CROSSREF
22. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475-81. PUBMED | CROSSREF
23. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol 2020;95:834-47. PUBMED | CROSSREF
24. Mantovani A, Rinaldi E, Zusi C, Beatrice G, Saccomani MD, Dalbeni A. Coronavirus disease 2019 (COVID-19) in children and/or adolescents: a meta-analysis. Pediatr Res 2021;89:733-7. PUBMED | CROSSREF
25. Henry BM, Benoit SW, de Oliveira MH, Hsieh WC, Benoit J, Ballout RA, et al. Laboratory abnormalities in children with mild and severe coronavirus disease 2019 (COVID-19): a pooled analysis and review. Clin Biochem 2020;81:1-8. PUBMED | CROSSREF
26. Folino F, Menis C, Di Pietro GM, Pinzani R, Marchisio P, Bosis S. Incidental occurrence of neutropenia in children hospitalised for COVID-19. Ital J Pediatr 2022;48:43. PUBMED | CROSSREF
27. Venturini E, Palmas G, Montagnani C, Chiappini E, Citera F, Astorino V, et al. Severe neutropenia in infants with severe acute respiratory syndrome caused by the novel coronavirus 2019 infection. J Pediatr 2020;222:259-61. PUBMED | CROSSREF
28. Husain EH, Mullah-Ali A, Al-Sharidah S, Azab AF, Adekile A. Infectious etiologies of transient neutropenia in previously healthy children. Pediatr Infect Dis J 2012;31:575-7. PUBMED | CROSSREF

요약

목적: 코로나19 판데믹이 시작된 이후, 다양한 주요 변이 바이러스가 출현했다. 코로나 19 판데믹 기간 동안 대표적인 주요 변이 바이러스 유행 시기를 네 가지로 나누고, 네 가지의 주요 변이 바이러스 시기로부터 임상적 그리고 혈액학적 검사의 특징을 파악하고자 하였다.
방법: 코로나19 확진으로 입원한 19세 이하 환자의 의무기록을 후향적으로 분석하였다. 변이전시기(2020년 2월 1일–2020년 9월 30일), 알파와 베타 변이 시기(2020년 10월 1일–2021년 5월 31일), 델타 변이 시기(2021년 6월 1일–2021년 10월 31일), 오미크론 변이 시기(2021년 11월 1일–2022년 5월 31일)를 비교하였다.
결과: 대상 환자 827명 중에서 163명(19.7%)가 무증상이었고, 발열과 기침의 빈도는 각각 320명(38.7%), 399명(48.2%)이었다. 38.5℃ 이상의 발열이 있었던 경우는 12세 미만인 경우에 오미크론 변이 시기에 높게 관찰되었다. 혈액학적 검사에서 백혈구 감소증, 임파구 감소증 그리고 호중구 감소증은 각각 33%, 30.2%, 24.9%로 관찰되었다.
결론: 코로나 19의 주요 변이 바이러스 우세 시기에 다른 특징들이 있었다. 델타 변이 시기에 4일 이상의 발열이 지속되는 경우가 더 많았고, 오미크론 변이 시기에는 38.5℃ 이상의 발열을 가지는 경우가 많았다.